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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/295,663	JOSHI ET AL.	
	Examiner	Art Unit	
	Joseph Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-44,46-54 and 69-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-44,46-54 and 69-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *16* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

File

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 15, 2002, paper number 15, has been entered.

DETAILED ACTION

This application, filed April 21, 1999, claims benefit to provisional applications: 60/082,665 filed April 22, 1998, 60/111,635 filed December 9, 1998, and 60/11,637 filed December 9, 1998.

Applicants' amendment filed January 15, 2002, paper number 17, has been received and entered. Claims 55-68 have been canceled. Claims 38, 47, 69, 74 and 77 have been amended. Claims 78-84 have been added. Claims 38-44, 46-54, 69-84 are pending and currently under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-44, 46-54, 69-77 stand rejected and newly added claims 78-84 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting the growth of cancer cells in a subject, the method comprising administering an amount of vincristine sulfate and cisplatin in an amount effective to inhibit growth of said cells at or around the site of the tumor, and administering to said cells a polynucleotide encoding a gene which is well known in the art to inhibit cell growth, does not reasonably provide enablement for a method of enhancing the therapeutic effect of a foreign gene administered to a patient.

Applicants summarize the instant invention as relating to methods for increasing the efficiency of transfection of cycling cells, wherein the cells are synchronized at a first stage of the cell cycle and transfection of the cell with a polynucleotide is performed at a second stage of the cell cycle. See Applicants' amendment, top of page 4. With respect to instant rejection, Applicants argue that undue experimentation is not necessary to practice the claimed invention citing *Ex parte Forman* and *In re Wands*. Applicants point out and summarize the teachings provided in the instant specification and note the working example provides a successful demonstration of providing expression of IL-12 for inhibition of tumor growth using the instantly claimed methods. Further, Applicants point out the specification discloses materials and methods to specifically target cells with antibodies and proteins linked to a lipid. See

Applicants' amendment, pages 5-7. Applicants' arguments have been fully considered but not found persuasive.

It is noted that the claims have been amended from a method of 'enhancing a therapeutic effect of a foreign therapeutic gene' to encompass a method of 'introducing a nucleic acid composition comprising a foreign therapeutic gene'. Though the instant claims do not recite or require that a therapeutic affect, or even that the polynucleotide be expressed, a review of the instant specification clearly teaches that the instantly claimed methods are directed to improved methods of gene therapy. Further, a review of the instant specification and the art of record does not provide any other use or teachings for the delivery of a therapeutic gene to a subject besides providing a therapeutic effect. Given that the only use disclosed for the instant methods is to affect treatment by gene therapy methodology, the instant claims must be read to encompass this limitation.

The instant claims are very broad encompassing the treatment of any type of cancer in a patient. Arguments that it would be routine experimentation to practice the claimed method are unpersuasive because the art recognizes that the available methodology and animals models do not adequately represent working models for use in humans. The specification provides a listing of types of cancers for possible treatment and general listing of genes which can be expressed, however the specification lacks the detailed guidance needed by the artisan to affect treatment. The instant specification fails to provide a nexus between the art recognized limitations for gene therapy protocols and the ability to successfully use or adapt the instantly claimed methods in

these protocols. Further, the present specification does not provide any guidance on how to create the numerous breadth of animal models needed to test, optimize and practice the invention as claimed. As noted in the previous office actions, Applicants working examples represent well known working examples in the art. The art recognizes the art of gene therapy is unpredictable, and the present specification fails to provide a nexus between the art recognized limitations known in the art and the means of routine experimentation to practice the claimed method for all types of cancer and with respect to new claims any possible therapeutic effect a patient may have. Examiner does not contend certain modes of delivery are not enabled for delivery of polynucleotide to a cell instead, that the present specification does not provide adequate guidance for one of ordinary skill in the art to practice the invention as claimed in the full breadth which when read in light of the specification is to provide a therapeutic effect. In addition, the breadth of the claims now encompass any form of gene therapy, however the specification is silent with the necessary guidance for the use of specific genes for specific diseases. Previously, Applicants specifically argued that Dachs *et al.*, Deonarian, Miller *et al.* and the present specification provides guidance and working examples of targeted gene delivery. The specification teaches only a liposome/protein compositions without the details of how to target a particular cell of interest. The mere recitation of various delivery vehicles does not provide adequate guidance for one of ordinary skill in the art to practice the invention. As pointed out in the cited references of record, the art recognizes the limitations of gene delivery and so because the present specification relies on the teachings of others for delivery, it also is presented with the same limitations

recognized in the art. The present specification fails to provide the necessary guidance needed to obtain the tissue specific delivery, or the necessary guidance for choosing the correct gene under the proper promoter for a therapeutic effect to treat cancer or any other disease encompassed by the claims. The reliance of the teachings of others and examples which reflect art recognized models present in the specification fails to provide the nexus and necessary guidance to overcome the art recognized limitations of gene therapy.

As previously noted each of Crystal, Orkin and Motulsky, Verma and Soia, each support the ability to deliver a specific nucleic acid to an organism and yield an effect, however, however each references point out that there has been limited success in the field of gene therapy, and the authors point out that the art recognizes that there are many limitations that still exist which limit the ability to routinely practice the methods gene therapy. As pointedly summarized by Verma and Somia "In principle, gene therapy is simple: putting corrective genetic material into cells alleviates the symptoms of disease. In practice, considerable obstacles have emerged." As discussed in detail in the previous office actions, there are several art recognized limitations and unpredictability issues regarding gene therapy, that include: vector to be used for gene expression, production of effective concentration of the candidate protein, delivery of the protein or gene to target cell, sustained expression and production of the candidate protein *in vivo*, and maintaining an effective level of the protein *in vivo*. Applicants specification relies in great part on the methods known in the art to practice the full scope of their invention and thus, are subject to the same limitations presently recognized in the art. For example, Examiner notes that the

specification discloses different viral vectors-adeno-, adeno-associated and retro-viral vectors used for gene therapy, however, as previously discussed above all these vector systems have limitations and the specification does not provide any guidance as to how an artisan would have addressed these limitations. The claimed invention requires the delivery of a polynucleotide to any cell in any organism as an essential element to practice claimed method, however the specification fails to provide a nexus between these many art recognized shortcomings of gene delivery to an organism and the practice of the full scope of the claimed invention.

Finally, Applicants have argued that in view of the art and the specification teachings, the claimed invention is predictable. However, the present teachings and examples of specification as instantly claimed do not differ from those presently found in the art, thus Applicants face the same shortcomings faced by others skilled in the art with regards to the specificity of cell targeting and the ability to regulate gene expression which would result in a desired effect. Applicants argue that the amount of experimentation is routine by a person of ordinary skill in the art. As previously noted by Applicants, the invention is not directed to a new method, nor specific vector for transforming cells, nor to a particular heat inducible promoter, nor a particular gene of interest, nor a particular host cell, and Examiner agrees that practice of the claimed method *in vitro* may require routine experimentation *in vitro*, however the claims encompass the practice of the method *in vivo*, and as such requires the presence and/or delivery of the a polynucleotide to any cancer cell within a subject, and new claims encompass the delivery to any cell for any desired therapeutic effect. Applicants have described a method for a potential

strategy to obtain increased therapeutic effect of a gene of interest however essentially all of the work required to ultimately develop the methods has been left for others. In the instant case, the specification is not enabling for the claimed invention because the arts of gene therapy are highly unpredictable as recognized in the prior art and because the specification as filed does not provide sufficient guidance, evidence and exemplification as to how an artisan would have carried out the claimed methods of controlling expression in any cell or organism, methods of therapy and would have addressed unpredictability issues as raised above, without undue experimentation.

Therefore, for the reasons above and of record, in view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention, it would have required one of skill in the art undue experimentation to practice the invention as claimed, and the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38-44, 46-54 and 69-77 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Amendments to and cancellation of claims has obviated the basis of the previous rejections, therefore the rejection is withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 38-44, 46, 47, 49, 52 and 69-73 rejected under 35 U.S.C. 102(b) as being anticipated by Roth *et al.* is withdrawn.

The claims have been amended to recite 'cell-cycle blocking agents selected from the group consisting of taxol, taxolene and a vinca alkaloid', and Applicants point out that Roth *et al.* do not teach these specific agents. See Applicants' amendments, pages 8-9. Applicants' arguments have been fully considered and found persuasive.

Upon review of Roth *et al.* Examiner agrees that the reference does not provide the specific teaching for the use of taxol, taxolene and a vinca alkaloid as cell cycle blocking agent, thus the teachings of Roth *et al.* do not anticipate the claims as newly amended. Therefore, the rejection is withdrawn.

Claims 38-44, 46, 47, 49, 52, 69-73 stand and newly added claims 79, 80, 81, 83 and 84 are rejected and under 35 U.S.C. 102(b) as being anticipated by Son *et al.*

The claims have been amended to recite 'cell-cycle blocking agents selected from the group consisting of taxol, taxolene and a vinca alkaloid', and Applicants point out that Son *et al.* do not teach each of these specific agents. Further, Applicants argue that Son *et al.* teach away from the present invention because though the vinca alkaloid vincristine is specifically taught, it was not found to be as effective as compared to cisplatin. See Applicants' amendments, pages 9-10. Applicants' arguments have been fully considered, but not found persuasive.

Examiner agrees that each taxol and taxolene are not taught, however as noted by Applicants, vincristine, a vinca alkaloid, is specifically taught. For anticipation, only a disclosure of the particular embodiments must be taught, and in the instant case, Son *et al.* teach the limitation of the vinca alkaloid vincristine for use in the instantly claimed methods. It is noted that the instant claims are not drawn to increased expression or transfection efficiencies, therefore, the methods disclosed in Son *et al.* anticipate the instant claims. Furthermore, Applicants' arguments directed to the lack of increased CAT enzyme activity demonstrated by Son *et al.* is unpersuasive, because upon review of the guidance given in the instant specification, the methodology of Son *et al.* would not differ from that instantly disclosed. Additionally, new claims 79, 80, 83 and 84 are dependent on claims 38 and 69, and are specifically drawn to a lipid formulation and the vinca alkaloid vincristine. Each of these limitations are taught by Son *et al.* Therefore, for the reasons above and of record, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 38, 53, 54 and 69-73 stand rejected and newly added claims 79, 80, 81, 83 and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roth *et al.* and Son *et al.*

As noted above, the claims have been amended to recite 'cell-cycle blocking agents selected from the group consisting of taxol, taxolene and a vinca alkaloid', and Applicants point out that neither Roth *et al.* nor Son *et al.* do not teach each of these specific agents. Further, Applicants argue that Son *et al.* teach away from the present invention because though the vinca alkaloid vincristine is specifically taught, it was not found to be as effective as compared to cisplatin. See Applicants' amendments, pages 10-11. Applicants' arguments have been fully considered, but not found persuasive.

Examiner agrees that each taxol and taxolene are not taught, however as noted by Applicants, vincristine, a vinca alkaloid, is specifically taught. In the instant case, Son *et al.* teach the limitation of the vinca alkaloid vincristine for use in the instantly claimed methods. It is noted that the instant claims are not drawn to increased expression or transfection efficiencies, therefore, the methods disclosed in Son *et al.* anticipate the instant claims as discussed above.

Furthermore, Applicants' arguments directed to the lack of increased CAT enzyme activity demonstrated by Son *et al.* is unpersuasive, because upon review of the guidance given in the instant specification, the methodology of Son *et al.* would not differ from that instantly disclosed. Furthermore, Son *et al.* do note an inconsistency with the results obtained in their experiments. In particular, carboplatin, an isomer of cisplatin, was known to be as effective as cisplatin in cancer treatment, however in the experiments provided a low effect on CAT activity (see page 12671, second column and figure 4). Son *et al.* propose that perhaps higher doses may be required for the same activity seen with cisplatin. Finally, new claims 79, 80, 81, 83 and 84 are dependent on claims 38 and 69, and are specifically drawn to a lipid formulation and the vinca alkaloid vincristine. Each of these limitations are taught by Son *et al.*

Thus, for the reasons above and of record, the claimed invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 38 and 48 stand rejected and newly added claims 78- 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Son *et al.,* Roth *et al.* and Walker *et al.*

As noted above, the claims have been amended to recite 'cell-cycle blocking agents selected from the group consisting of taxol, taxolene and a vinca alkaloid', and Applicants point out that neither Roth *et al.* nor Son *et al.* do not teach each of these specific agents. Further, Applicants argue that Son *et al.* teach away from the present invention because though the vinca alkaloid vincristine is specifically taught, it was not found to be as effective as compared to

cisplatin. Further, given these deficiencies, one would not be motivated to combine nor do the teachings of Walker *et al.* cure the deficiencies to provide the invention as instantly claimed. See Applicants' amendments, pages 11-12. Applicants' arguments have been fully considered, but not found persuasive.

Examiner agrees that each taxol and taxolene are not taught, however as noted by Applicants, vincristine, a vinca alkaloid, is specifically taught. In the instant case, Son *et al.* teach the limitation of the vinca alkaloid vincristine for use in the instantly claimed methods. It is noted that the instant claims are not drawn to increased expression or transfection efficiencies, therefore, the methods disclosed in Son *et al.* anticipate certain claims as discussed above. Furthermore, Applicants' arguments directed to the lack of increased CAT enzyme activity demonstrated by Son *et al.* is unpersuasive, because upon review of the guidance given in the instant specification, the methodology of Son *et al.* would not differ from that instantly disclosed. Furthermore, Son *et al.* do note an inconsistency with the results obtained in their experiments. In particular, carboplatin, an isomer of cisplatin, was known to be as effective as cisplatin in cancer treatment, however in the experiments provided a low effect on CAT activity (see page 12671, second column and figure 4). Son *et al.* propose that perhaps higher doses may be required for the same activity seen with cisplatin. Clearly Son *et al.* indicate that the evidence presented is not consistent nor complete, and provide motivation to attempt other concentrations of the compound described. Walker *et al.* was introduced to teach the limitation that the liposome contain a secondary agent, in this case a 'cell cycle blocking agent'. It was known in

the art, as noted in both Roth *et al.* and Son *et al.*, liposomes are known vehicles for the delivery of polynucleotides. In addition, it is well known in the art that other compounds can and are delivered by means of a liposome carrier, and Walker *et al.* was introduced to provide an example of this teaching. Specifically, Walker *et al.* disclose the systemic delivery of agents by means of a liposome. Clearly, each reference contains teachings for the delivery of liposomes for treatment, and though Roth *et al.* does not provide a specific example, the specification does teach that 'the DNA damaging agent may be prepared and used in combined therapeutic compositions, or kit, by combining it with a p53 protein, gene or gene delivery system' clearly indicating that Roth *et al.* appreciated that various combinations of polynucleotides and agents could be combined for more effective treatment. Each reference provides the motivation of utilizing liposomes in combination with a polynucleotide or an agent. Each provide working examples and provide adequate guidance in the method sections for one of ordinary skill in the art to reproduce the teachings. Claims 78 and 82 are included in the basis of this rejection because the teachings of Walker *et al.* provide the guidance for the making and optimization of lipid formulations which would make obvious these claims. Finally, new claims 79, 80, 81, 83 and 84 are dependent on claims 38 and 69, and are included in the instant rejection because they are specifically drawn to a lipid formulation and the vinca alkaloid vincristine. Each of these limitations are taught by Son *et al.*

Thus, for the reasons above and of record, the claimed invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 74-77 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Roth *et al.* and Son *et al.* as applied to claims 38, 53-73 above, and further in view of Bally *et al.*

As noted above, the claims have been amended to recite 'cell-cycle blocking agents selected from the group consisting of taxol, taxolene and a vinca alkaloid', and Applicants point out that neither Roth *et al.* nor Son *et al.* do not teach each of these specific agents. Further, Applicants argue that Son *et al.* teach away from the present invention because though the vinca alkaloid vincristine is specifically taught, it was not found to be as effective as compared to cisplatin. Further, given these deficiencies, one would not be motivated to combine nor do the teachings of Bally *et al.* cure the deficiencies to provide the invention as instantly claimed. See Applicants' amendments, pages 12-13. Applicants' arguments have been fully considered, but not found persuasive.

Newly amended claims 74-77 encompass a method for treating a patient having cancer comprising administering a cell cycle blocker to a patient, and administering a therapeutic gene wherein the gene is in a lipid formulation consisting of PEG-lipid derivative (PEG-ceramide-C14, -C20 and -C8)and a Gm1-modified lipid.

Arguments as they pertain to the rejection over Roth *et al.* and Son *et al.* are summarized above. Briefly, Son *et al.* teach the limitation of the vinca alkaloid vincristine for use in the instantly claimed methods. Further, Applicants' arguments directed to the lack of increased CAT enzyme activity demonstrated by Son *et al.* is unpersuasive, because upon review of the guidance given in the instant specification, the methodology of Son *et al.* would not differ from that

instantly disclosed. In addition, Son *et al.* do note an inconsistency with the results obtained in their experiments. In particular, carboplatin, an isomer of cisplatin, was known to be as effective as cisplatin in cancer treatment, however in the experiments provided a low effect on CAT activity (see page 12671, second column and figure 4). Son *et al.* propose that perhaps higher doses may be required for the same activity seen with cisplatin. It is acknowledged that Roth *et al.* and Son *et al.* teach various liposome compositions however they do not teach the specific lipid composition comprising a PEG-lipid derivative and a Gm1-modified lipid. However, Bally *et al.* teach lipid-nucleic acid particles for the delivery and use in gene transfer, in particular the use of PEG-lipid derivative and a Gm1-modified lipids to prevent particle aggregation (columns 12-13; bridging paragraph). The experiments of Son *et al.* indicate that optimization for the administration of compounds may be necessary in view of the results with carboplatin. Bally *et al.* provide another means for optimization of delivery. (Bally, column 13; lines 1-7). There would have been a reasonable expectation of success given the results of Roth *et al.* and Son *et al.* to deliver a polynucleotide with the liposomes specifically disclosed therein, and substitute the various lipid compositions taught by Bally *et al.* to optimize delivery of the polynucleotide to a particular cell type to reproduce the disclosed method of enhancing delivery and therapeutic effect of the gene.

Thus, the claimed invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

A prior art reference made of record but not relied upon in the instant office action:

Lee *et al.*, Cancer Research 56:1302-1308, March 15, 1996, provide evidence that at the time of filing other anti-cancer agents were known and used. Specifically, taxol was an anti-cancer compound was known in the art and demonstrated to have the activity of stabilizing microtubules and blocking cell mitosis (page 1303, first paragraph).

Conclusion

No claim is allowed.

All claims are drawn to the same invention claimed in the parent application prior to the filing of this request for continued examination under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing under 37 CFR 1.53(d). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will

the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Patsy Zimmerman whose telephone number is (703)308-8338.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800/1630